Medicaid Policy Number (This number will be generated by Medical Services.)	Date Policy was Last Reviewed
NDMP-2012-0006	06/15/2015

Title
Gene Expression Profiling for Breast Cancer (Oncotype DX, MammaPrint)

Effective Date
March 1, 2012

Revision Date(s)
June 15, 2015

Replaces

Cross References

Description
The application of gene expression profiling using Oncotype Dx is employed to identify patients who are predicted to obtain the most therapeutic benefit from adjuvant tamoxifen and may not require adjuvant chemotherapy. The absolute benefit of chemotherapy depends on the baseline risk of recurrence. Conventional risk classifiers estimate recurrence risk by considering criteria such as the tumor size, type, grade, and histologic characteristics; hormone receptor status; and lymph node status.

Scope
Five gene expression tests are commercially available in the United States: Oncotype Dx (a 21-gene RT-PCR assay; Genomic Health), the 70-gene signature MammaPrint (also referred to as the "Amsterdam signature"; Agendia), "Mammostrat" (developed by Applied Genomics Inc. and currently offered by the Molecular Profiling Institute), the Molecular Grade Index (Aviara MGI; AviaraDx, Inc.) and the Breast Cancer Gene Expression Ratio (as originally offered by Quest Diagnostics under license; currently offered by AviaraDx; Inc. as Aviara H/I). If these panels are more accurate than current conventional classifiers, they could be used to aid in chemotherapy decision-making and overall survival outcomes.

Policy
ND Medicaid will consider the the application of gene expression profiling using the Oncotype Dx as medically reasonable and necessary, with case by case review as needed, when used to assess the need for adjuvant chemotherapy in patient with recently diagnosed breast cancer (six months or less have elapsed) when all of the following criteria are met:

1. Breast cancer is nonmetastatic (node-negative) (lymph nodes with micrometastases are not considered positive); and
2. Breast cancer is unilateral and non-fixed (i.e., tumor not adhered to chest wall); and
3. Breast tumor is hormone receptor-positive (estrogen receptor (ER)-positive or progesterone receptor (PR)-positive); and
4. Breast tumor is HER2-receptor negative; and
5. Breast tumor size is 0.6-1 cm with moderate/poor differentiation or unfavorable features (e.g., angiolymphatic invasion, high nuclear grade, or high histologic grade), OR tumor size is >1 cm; and
6. Breast tumor is stage I or stage II; and
7. Breast cancer will be treated with hormonal therapy; and
8. Adjuvant chemotherapy is not precluded due to any other factor (e.g., advanced age and/or significant co-morbidities); and

9. Testing is being done specifically to guide the decision as to whether or not adjuvant chemotherapy will be used and, prior to testing the patient and oncologist have discussed the potential results of the test and agree to the use the results to guide therapy (i.e., the patient will forgo the adjuvant chemotherapy if Oncotype DX score is low; chemotherapy is a therapeutic option).

**Medical tests are covered only when ordered by the treating oncologist, when necessary for diagnosis or treatment decisions, and when used in patient care (42 CFR 410.32).

Policy Guidelines

The 21-gene RT-PCR assay Oncotype Dx should only be ordered after surgery and subsequent pathology examination of the tumor have been completed. The test should be ordered in the context of a provider-patient discussion regarding risk preferences when the test result will aid in making decisions regarding chemotherapy.

All other uses of Oncotype Dx are considered experimental or investigational; specifically the following indications:

1. To predict response to specific chemotherapy regimens
2. Repeat Oncotype Dx testing or testing of multiple tumor sites in the same patient

In a clinical trial, this test would typically be used for data collection and would not be considered a routine cost and, therefore, this service would not be billed.

Gene Expression Profiling as a technique of managing the treatment of breast cancer is considered infestigational and not medically necessary when a gene profiling test other than the Oncotype Dx breast cancer assay is used, including but not limited to:

1. Breast Cancer Gene Expression Ratio
2. MammaPrint
3. Rotterdam 76-Gene Signature
4. The 41-gene signature assay
5. Amsterdam 70-Gene Profile

ND Medicaid does not allow/reimburse services that are experimental or investigational.

Benefit Application

The following documentation should be available for review upon request:

1. Patient history and physicial
2. Pathology report
3. Documentation which indicates all of the following:

A. The results of the Oncotype Dx test are expected to play a significant role in management of the patient

B. The patient is a candidate for possible adjuvant chemotherapy and testing is being done specifically to guide the decision as to whether or not adjuvant chemotherapy will be used

C. The genomic information derived from this test has been integrated with copathological paramenters, such as patient age and functional status, comorbidities and tumor grade.

Rationale Source

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Huang, C., & Bredel, M. (2008). Use of gene signatures to improve risk estimation in cancer. JAMA, 299(13), 1605-1606.

Lyman, G., Cosler, L., Kuderer, N., & Hornberger, J. (2007). Impact of a 21-gene RT-PCR assay on treatment decisions in early-stage breast cancer. Cancer, 109(6), 1011-1018.

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Code of Federal Regulations Citation(s)

42 CFR 410.32; 42 CFR 410.42

CODES	NUMBER	DESCRIPTION
CPT®	84999	Unlisted Chemistry Procedure
Applicable Modifier(s)	N/A	N/A
ICD-9 Diagnosis(es)	174.0-174.9	Malignant neoplasm of nipple and areola of female breast - malignant neoplasm of breast (female) unspecified site
	175.0-175.9	Malignant neoplasm of nipple and areola of male breast - malignant neoplasm of other and unspecified sites of male breast
	V86.0*	Estrogen receptor positive status (ER+) **ICD-9 code V86.0 is a secondary diagnosis code and should not be billed as the primary diagnosis; therefore, this diagnosis code (V86.0) must be billed with another diagnosis code from the list above
ICD-10 Diagnosis(es)	C50.011	Malignant neoplasm of nipple and areola, right female breast
	C50.012	Malignant neoplasm of nipple and areola, left female breast
	C50.111	Malignant neoplasm of central portion of right female breast
	C50.112	Malignant neoplasm of central portion of left female breast
	C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
	C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
	C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
	C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
	C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
	C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
	C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
	C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
	C50.611	Malignant neoplasm of axillary tail of right female breast

	C50.612 C50.811 C50.812 C50.911 C50.912 C50.021 C50.022 C50.121 C50.122 C50.221 C50.222 C50.321 C50.322 C50.421 C50.422 C50.521 C50.522 C50.621 C50.622 C50.821 C50.822 C50.921 C50.922 Z17.0	Malignant neoplasm of axillary tail of left female breast Malignant neoplasm of overlapping sites of right female breast Malignant neoplasm of overlapping sites of left female breast Malignant neoplasm of unspecified site of right female breast Malignant neoplasm of unspecified site of left female breast Malignant neoplasm of nipple and areola, right male breast Malignant neoplasm of nipple and areola, left male breast Malignant neoplasm of central portion of right male breast Malignant neoplasm of central portion of left male breast Malignant neoplasm of upper-inner quadrant of right male breast Malignant neoplasm of upper-inner quadrant of left male breast Malignant neoplasm of lower-inner quadrant of right male breast Malignant neoplasm of lower-inner quadrant of left male breast Malignant neoplasm of upper-outer quadrant of right male breast Malignant neoplasm of upper-outer quadrant of left male breast Malignant neoplasm of lower-outer quadrant of right male breast Malignant neoplasm of lower-outer quadrant of left male breast Malignant neoplasm of axillary tail of right male breast Malignant neoplasm of axillary tail of left male breast Malignant neoplasm of overlapping sites of right male breast Malignant neoplasm of overlapping sites of left male breast Malignant neoplasm of unspecified site of right male breast Malignant neoplasm of unspecified site of left male breast Estrogen receptor positive status [ER+] **ICD-10 code Z17.0 should not be billed as the primary diagnosis; therefore, this diagnosis code (Z17.0) must be billed with another diagnosis code from the list above
Applicable Revenue Codes(s)	301	Laboratory - Chemistry
HCPCS Code(s)	S3854	Gene expression profiling panel for use in the management of breast cancer treatmen
Type of Service	Laboratory	Inpatient/Outpatient Hospital
Place of Service	81	Independent Laboratory